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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/099,823	06/19/1998	PATRICIA A. BILLING-MEDEL	6120.US.P1	7897

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ABBOTT LABORATORIES
DEPT. 377 - AP6D-2
100 ABBOTT PARK ROAD
ABBOTT PARK, IL 60064-6050

EXAMINER
GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/08/2002

29

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/099,823	BILLING-MEDEL ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-29,31,32,34,36,37,43,44 and 50-74* is/are pending in the application.

4a) Of the above claim(s) *17-29,31,32,34,36,37,43 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed March 29, 2002. Currently, claims 17-29, 31-32, 34-36, 37, 43-44, 50-74 are pending. Claims 17-29, 31-32, 34, 36-37, 43-44 have been withdrawn from consideration. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow.

2. Any objections and rejections not reiterated below are hereby withdrawn.

3. This action is FINAL.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 50-74 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

Definitions: [from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]

> "Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such

use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring.

On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a

"real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. ' 101. This analysis should, or course, be tempered by consideration of the context and nature of the invention. For example, it a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.

5. The claims drawn to polynucleotides, and method of detecting the polynucleotides in a test sample as defined in the specification as products of a breast tissue gene designated as BS124. The specification teaches the general utility for the invention is detection of the gene product itself in a sample. The specification does not teach a specific utility of the polynucleotides, genes and proteins whereby the invention would be a useful tool for a specific purpose i.e. detection of itself in a sample detects the presence of a disease. The specification also does not provide any teachings as to the function of the encoded protein. The specification suggests that the invention may have substantial utility i.e. as an anti-BS124 antibody useful as a therapeutic agent. However, the specification does not teach the therapy or demonstrate therapeutic results. Additionally, the specification suggests that the invention may have substantial

utility i.e. the gene products may be useful for the diagnosis of breast cancer by using the gene products to detect themselves in a tissue sample by hybridization. However, the specification does demonstrate the diagnostic utility. Specifically, the specification teaches that the claimed gene products detect themselves in cancerous breast tissue. Additionally, the specification teaches that the BS124 was found in non-breast libraries. Similarly, BS124 sequences were observed in normal breast tissue RNAs and breast cancer tissue RNAs. Therefore, the specification does not teach a specific or substantial utility for the invention such that the invention would be useful to detect or treat a disease state. While the utility of gene products has been established in the art, applicants have not demonstrated a specific or substantial utility for the claimed invention.

Response to Arguments

The response traverses the rejection. The response asserts that the BS124 is a novel polypeptide belonging to the lipocalin family which serve as transfer molecules and provides post filing date support including the reference by Lacazette which was previously considered. As provided in the Office Action mailed September 14, 2000, lipocalin-encoding" was not part of the original specification and disclosure. It is noted that utility is required at the time of filing. Therefore, support for the utility after the filing date of the invention does not illustrate that at the time the invention was made the specification provided how to use the claimed invention.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 50-74 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 50-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification provides numerous assays and results with regard to detection of "the BS124 probe". It is unclear however, what this probe includes. It is unclear whether this probe is the entire SEQ ID NO: 5 or whether the probe is a smaller fragment of 5, or whether numerous probes were used. Clarification is requested.

The specification teaches "EST's corresponding to the consensus sequence of BS124 were found in 5.9% (2 of 34) of breast tissue libraries (pg 57, lines 21-23). The specification further teaches that EST's corresponding to the consensus sequence of SEQ ID NO: 5 or fragments thereof were only found in 0.3% of the other non-breast libraries of the database (pg 57, lines 23-25).

The specification teaches that RNA was isolated from breast tissue and from non-breast tissue (pg 59). The specification teaches performing an RNA protection assay (pg 62-64). The specification teaches that the RNA was mixed with labeled probe, however, it is unclear what the sequence of this probe entailed (pg 63, lines 6-8). The gels were imaged and analyzed and quantitation of protected fragment bands was achieved. Results of the assay indicated that four of five of the normal breast tissues had detectable bands, whereas three of the six breast cancer samples had detectable bands. This appears to clearly illustrate that the BS124 nucleic acids is present in both normal and cancerous samples. While it is noted that the quantification of the nucleic acids from the normal samples appeared lower on several samples than the cancerous samples, the BS124 nucleic acid appears in more normal samples than cancerous samples (Table 1, page 64).

The specification teaches Northern Blotting to identify a specific size RNA species. It remains unclear what probe was used in the assay. However, it appears clear that the probe was detected in the normal testis (Figure 3A). From Figure 3B it also appears as though the probe was detected in two of six breast cancer samples.

The specification also describes an RT-PCR assay in which shows a "100 bp BS124-specific PCR amplification product in lanes 3-11, indicating that BS124 mRNA was present in 9 or 10 normal and breast cancer samples tested" (pg 69, lines2-5). Turning to Figure 4A, it is clear that all five of the normal samples contained the BS124 mRNA, however, one of the breast cancer samples did not. The specification also provides that the 100 bp BS124 specific PCR amplification product is observed (faintly)

in normal lung sample (Figure 4B). The specification suggests that BS124 is breast specific (pg 69, line 6).

Neither the specification nor the art teaches how to make and use the invention as broadly as claimed. The claims are directed to detecting a polynucleotide indicative of breast cancer. The specification asserts that BS124 is breast specific, however the detection of a BS124 polynucleotide has been identified in testis, normal breast tissue, cancerous breast tissue and normal lung samples using the various assays described. Moreover, with respect to the instant claims drawn to detecting polynucleotides indicative of breast cancer, the specification provides several assays including, RT-PCR assays and RNAase Protection Assays. It is unpredictable for the skilled artisan to detect a polynucleotide indicative of breast cancer using the instant nucleic acids because the instant nucleic acids are not indicative of breast cancer. Based upon the teachings in the specification, the instant nucleic acids are do not appear indicative of breast cancer.

Therefore, the skilled artisan would be unable to use the claimed methods and products.

Response to Arguments

The response traverses the rejection. The response asserts that the BS124 is a novel polypeptide belonging to the lipocalin family which serve as transfer molecules and provides post filing date support including the reference by Lacazette which was previously considered. As provided in the Office Action mailed September 14, 2000, lipocalin-encoding" was not part of the original specification and disclosure. It is noted

that utility is required at the time of filing. Therefore, support for the utility after the filing date of the invention does not illustrate that at the time the invention was made the specification provided how to use the claimed invention.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112- Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 68-69, 74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polynucleotides having a sequence selected from the group consisting of SEQ ID NO: 4 and 5 (Claim 69). The claims are also drawn to a composition of matter comprising a polynucleotide selected from the group consisting of SEQ ID NO: 1, 2, 4, 5 (Claims 68, 74).

The specification teaches the polynucleotides consisting of SEQ ID NO: 1-5. The specification teaches a single BS124 consensus polynucleotide, SEQ ID NO: 5, the sequence of which was assembled from 3 EST clones (SEQ ID NO:1-3) and the fill-length clone (SEQ ID NO: 4) (pg. 57).

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its ennoblement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of specifies have been described by their complete structure. In the instant case, Applicant has defined only a fragment of a nucleic acid

sequence. Applicant has not disclosed any genomic DNA sequences and particularly has not disclosed any intron sequences or regulatory sequences. Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

There is not adequate description of the genus of polynucleotides having SEQ ID NO: 4 or 5 and compositions of matter comprising SEQ ID NO: 1, 2, 4, 5. These claims encompass the full length gene, the full length cDNA molecules which have not been described. Thus, the claims have not provided a representative number of species within the genus claimed.

Response to Arguments

The response does not appear to address the written description rejection. Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

8. No claims allowable.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of formal matters can be directed to the patent analyst, Chantae Dessau, whose telephone number is (703) 605-1237.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Goldberg
April 4, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600